

**REMARKS**

Claims 1-85 were originally filed in the present application. Claims 1-81 have been withdrawn from further consideration by the examiner as being drawn to non-elected inventions. Claims 82-85 are pending and have been examined on the merits. Applicants have amended the specification to include the omitted text of Example 4. No new matter has been added. Attached hereto is a marked-up version of the changes made to the specification and claims by the present amendment. The attached page is captioned "**Version with markings to show changes made**".

As a preliminary matter, Applicants respectfully request that the Attorney Docket Number **ORT-1296** be changed to **PRI-0013 (ORT-1296)** for all future correspondence. Applicants acknowledge that the IDS filed January 29, 2001 (Paper 34) is complete as one page (Sheet 1) and thank Examiner for acknowledging the same.

Applicants also enclose herewith an Associate Power of Attorney and Change of Correspondence Address recently filed in connection with this application. The examiner is requested to forward all future correspondence to the undersigned attorney at the new correspondence address.

**Rejection under 35 USC §112 ¶2**

Claims 82-85 are rejected as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter of the invention. Claims 82-85 depend from non-elected inventions and are therefore deemed indefinite because the elected invention of claims 82-85 is not found within these claims.

Applicants have amended claims 82-85 to include the limitations set forth in the non-elected claims from which they depend, and hence the elected invention particularly points out and distinctly claims the subject matter of the invention. As such, the examiner's rejection should be overcome and Applicants respectfully request that it be withdrawn.

Claims 82 and 84 are also rejected on the basis that the term "discovered" is not clear, for claims from which claims 82 and 84 depend are drawn to method claims for use of a compound to determine its effect on gene expression, and not the discovery of a compound. Claims 82 and 84 have been amended such that the term "discovered" no longer appears in the claims. As such, the examiner's rejection should be overcome and Applicants respectfully request that it be withdrawn.

#### **Rejection under 35 USC §102(b)**

Claims 82-85 are rejected under 35 USC §102(b) as being anticipated by Mazer et al. (U.S. Patent No. 5,698,222). According to the examiner, the Mazer patent teaches a calcium supplement in a pharmaceutical formulation and thereby anticipates the claims of Applicants' invention. Applicants respectfully traverse the rejection and seek reconsideration and withdrawal of the rejection.

A claim is anticipated only if each and every element of the claim is present either expressly or inherently in a single prior art reference. *MPEP* § 2131. The Mazer patent fails to anticipate each and every element of the claimed invention. The Mazer patent

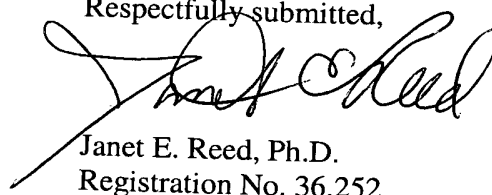
merely discloses a solid calcium supplement wherein the form of calcium present in the supplement is calcium glycerophosphate. It does not disclose a transcription factor regulator identified through the steps of contacting a compound suspected of being a transcription factor regulator with a cell having a nucleus and containing a membrane-bound, constitutively active transcription factor; activating a protease to release the transcription factor from the membrane, thereby allowing the transcription factor to translocate to the nucleus; and measuring the resultant gene expression under promotional control of the membrane bound transcription factor. Nor does it disclose a pharmaceutical composition comprising a transcription factor regulator that is identified in the manner claimed. The present invention is directed to an organic or inorganic compound that has the potential to modulate the specific response of an extracellular ligand by competitive or noncompetitive means. This compound may include, but is not limited to, small organic or inorganic molecules, synthetic or natural amino acid polypeptides, proteins including monoclonal antibodies, or synthetic or natural nucleic acid compounds. Even assuming that calcium is a protease activator which in turn stimulates a protease to release a transcription factor from the membrane, this activity is not disclosed by the Mazer patent. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection.

It is the Applicants' understanding that the Yamamoto, et al. patent (U.S. Patent No. 5,053,333) was cited by the Examiner as art of record and not as the basis for a rejection.

**Conclusion**

In view of the amendments submitted herewith and the foregoing remarks, the presently pending claims are believed to be in condition for allowance. Applicants respectfully request early and favorable reconsideration and withdrawal of the objections and rejections set forth in the July 12, 2002 Official Action, and allowance of this application.

Respectfully submitted,

A handwritten signature in black ink, appearing to read "Janet E. Reed", is written over the typed name.

Janet E. Reed, Ph.D.

Registration No. 36,252

Date: 11/7/2002

WOODCOCK WASHBURN LLP  
One Liberty Place- 46<sup>th</sup> Floor  
Philadelphia, PA 19103  
(215) 568-3100

VERSION WITH MARKINGS TO SHOW CHANGES MADE

**In the Specification**

At page 35, line 7, the paragraph has been amended as follows:

As illustrated in Figure 4, induction of alkaline phosphate mRNA in an assay of the invention using the estradiol-inducible zinc finger was measured.

**In the Claims**

The claims have been amended as follows:

82. A transcription factor regulator identified by a [compound discovered using the] method comprising the steps of: [claim 72]
- a) contacting a compound suspected of being a transcription factor regulator with a cell having a nucleus and containing a membrane-bound, constitutively active transcription factor produced by expression of a nucleic acid construct comprising an expression vector containing:
    - i) a constitutively active domain;
    - ii) a synthetic DNA binding domain that binds to a nucleic acid sequence and activates transcription of an endogenous gene; and
    - iii) a membrane anchoring domain that contains a protease cleavage site, wherein the constitutively active domain is operably linked to the DNA binding domain such that the transcription factor is active in an unregulated fashion;

b) stimulating activity of a protease by the compound to release the transcription factor from the membrane, thereby allowing the transcription factor to translocate to the nucleus; and

c) measuring expression of a gene under promotional control of the membrane-bound transcription factor, whereby an increase or decrease in expression of the gene is indicative that the compound is a transcription factor regulator.

83. A pharmaceutical composition comprising a transcription factor regulator of claim 82 [compound of claim 83].

84. A transcription factor regulator identified by a [compound discovered using the] method comprising the steps of: [claim 73]

a) contacting a compound suspected of being a transcription factor regulator with an extracellular ligand and a cell having a nucleus and containing a membrane-bound, constitutively active transcription factor produced by expression of a nucleic acid construct comprising an expression vector containing:

i) a constitutively active domain;

ii) a synthetic DNA binding domain that binds to a nucleic acid sequence and activates transcription of an endogenous gene; and

iii) a membrane anchoring domain that contains a protease cleavage site, wherein the constitutively active domain is operably

linked to the DNA binding domain such that the transcription factor is active in an unregulated fashion;

b) stimulating activity of a protease by either the compound or the ligand to release the transcription factor from the membrane, thereby allowing the transcription factor to translocate to the nucleus; and  
c) measuring expression of a gene under promotional control of the membrane-bound transcription factor, whereby an increase or decrease in expression of the gene is indicative that the compound is a transcription factor regulator.

85. A pharmaceutical composition comprising a transcription factor regulator [compound] of claim 84.